Molecular Self-organization and the Origin of Life: Formation and Functions of Protocells

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1. Unassisted Ion Transport across Membranes

Unassisted transport across membranes is the most likely mechanism by which ions moved across walls of protocells. This process requires considerable energy of activation. This energy for Na^+, estimated from the continuum electrostatic model at 46 kcal/mol, yields a membrane permeability of 10^{-28} cm s^{-1}, compared to the measured values of 10^{-13} to 10^{-15} cm/sec. The origin of this large discrepancy was studied by molecular dynamics simulations in which either a Na^+ or Cl^- ion was moved across the glycerol 1-monooleate membrane. As the ion moves into the interior of the bilayer, it creates a local disruption in the membrane, whereby water molecules and polar head groups follow the ion into the nonpolar core. The disruption of the membrane is asymmetric - perturbations of the structure are localized mostly on one side of the bilayer. The disruption reduces the activation energy by approximately 40%. This increases membrane permeability to Na^+ by 16 orders of magnitude. Cl^- is transferred somewhat faster due to favorable interactions with the electric field at the membrane–water interface. These results are in good agreement with experimental values.

2. Transport of Small, Neutral Solutes across Membranes

Among small neutral solutes whose unassisted transport across membranes is of protobiological interest are metabolites, building blocks of biopolymers, protonophores and

potential pigments. To determine the concentrations of solutes as a function of their position in the bilayer, and to elucidate the mechanism of their transport across the membrane, the free energy profiles for the transfer of 1,1,2-trifluoroethane (TFE) and perfluoroethane (PFE) across the GMO bilayer were calculated. The main difference between these structurally similar molecules is their polarity. TFE is fairly polar and is soluble in both water and oil whereas PFE is nonpolar and dissolves well in oil but very poorly in water.

The free energy profiles for the transfer of TFE and PFE across the water–membrane interface differ considerably. The free energy profile for PFE decreases sharply toward the membrane interior whereas the profile for TFE exhibits a broad minimum in the head group region of the bilayer. Thus, the highest concentration of PFE is in the interior of the bilayer whereas the highest concentration of TFE is near the surface of the membrane.

Our calculations allow for drawing a general conclusion that molecules exhibiting sufficient hydrophilicity and hydrophobicity accumulate near the surface of the membrane, even if they do not possess amphiphilic structure. This property is determined primarily by the polarities of the phases in contact and, therefore, our conclusion also applies to interfaces between water and oil slicks. Some surface active molecules could be of special protobiological interest because of their potential catalytic or energy capturing capabilities. Transport across membranes is, in general, more complicated than assumed by the conventional solubility–diffusion model. In particular, molecules which accumulate at the interface experience "interfacial resistance" to transfer across membrane-water interface.

3. Interactions of a Model Dipeptide with the Membrane–Water and Water–Oil Interfaces

Since simple, membrane–bound peptides are candidates for the earliest enzymes and transmembrane channels, understanding the principles which determine their organization is an important goal in studies of the origin of life. Probably the simplest model for studying conformational preferences in peptides is alanine dipeptide. Stable conformations of this

molecule depend on the environment in which it is located. The conformations in the gas phase and in nonpolar solvents (e.g. hexane) are stabilized by intramolecular hydrogen bonds. In contrast, these hydrogen bonds are no longer stable in water, and alanine dipeptide adopts conformations characterized by torsional angles typical of α-helices and β-sheets in proteins.

Extensive molecular dynamics simulations show that alanine dipeptide exhibits a deep free energy minimum at the water–hexane and water–membrane interfaces. Conformations identified in both, water and hexane are all stable at the interfaces. Furthermore, the energy barriers between different conformations are markedly reduced, compared to those in the corresponding bulk phases. As a result, the rate of isomerization between α and β conformations at the interface is 15 times faster than that in bulk water.

The results of our work have been described in eight papers.